My patient is iron deficient: what's next?

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Disclosures

I received speakers honorarium from:

Actelion, AstraZeneca, Novartis, Pfizer, Servier, Vifor

I received consulting fees from:

MSD, Novartis, Pfizer, Servier, Vifor

Case: 45 year old male patient

- **Non-ischemic cardiomyopathy 2006**
  - DD: post-inflammatory, idiopathic, arrhythmogenic
  - Severely reduced left ventricular ejection fraction (LVEF: 30%)
  - Functional mitral regurgitation (Grade II)
  - Moderately decreased right ventricular function (FAC 21%, TAPSE 12)
  - Postcapillary pulmonary hypertension
  - CRT-ICD 2007
  - Peak VO2 18ml/min/kg (2008)
  - Permanent atrial fibrillation
  - cvRF: tabbaco use,
- **Chronic kidney disease, Stage III**
  - Cardio-renal Syndrom, GFR (MDRD): 47 ml/kg/1.73 m2
- **Sleep apnea**
  - CPAP
- **Non-insulin dependent diabetes mellitus (NIDDM)**

Medication

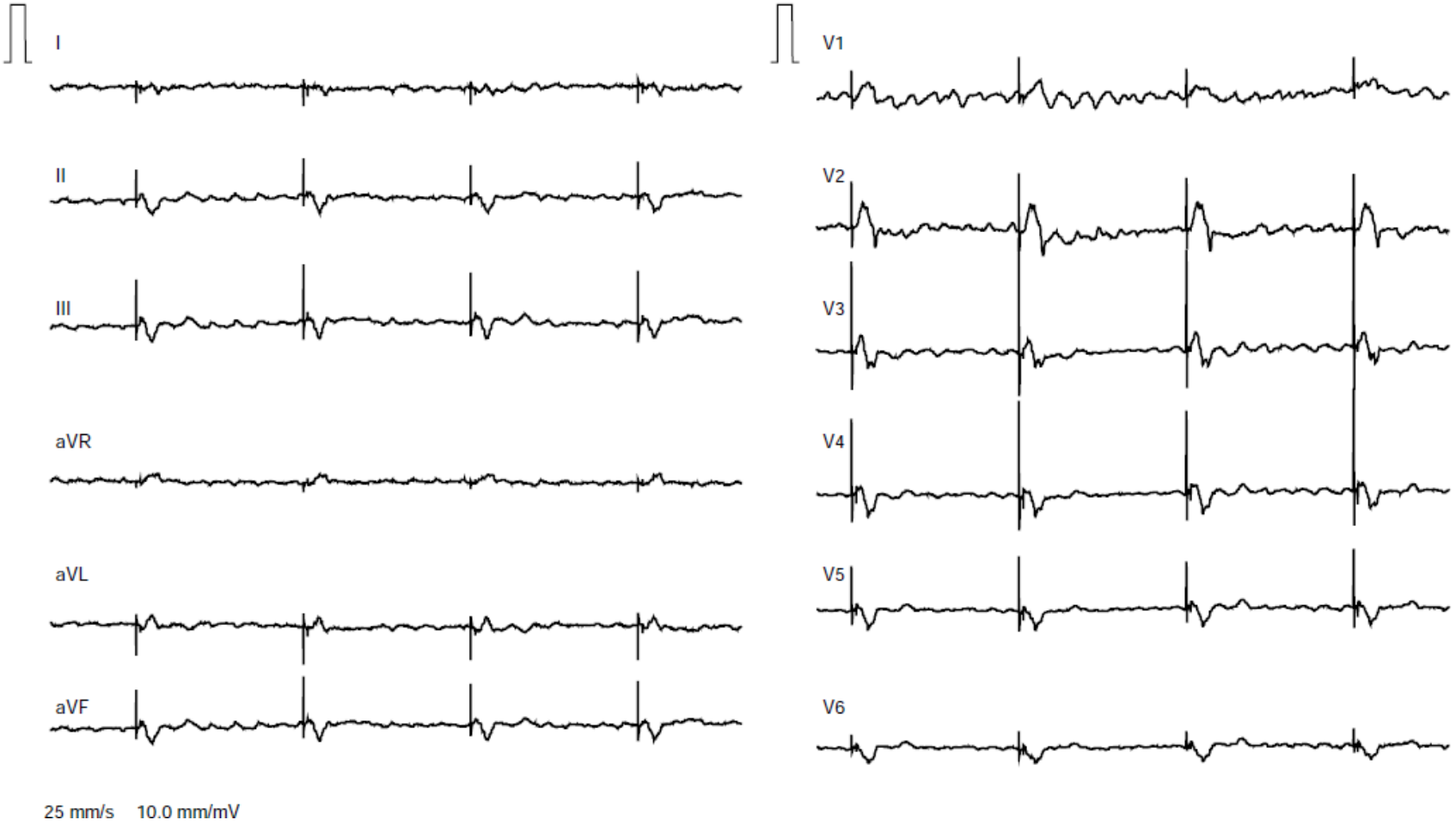
- Perindopril (5mg) 1 - 0 - 1
- Carvedilol (25mg) ½ - 0 - 1
- Eplerenone (25mg) 1 – 0 - 0
- Digoxin (0.125mg) 1 – 0 - 0
- Torasemid (10mg) 1 – 0 - 0
- Phenprocoumon (Marcoumar)

Current medical history

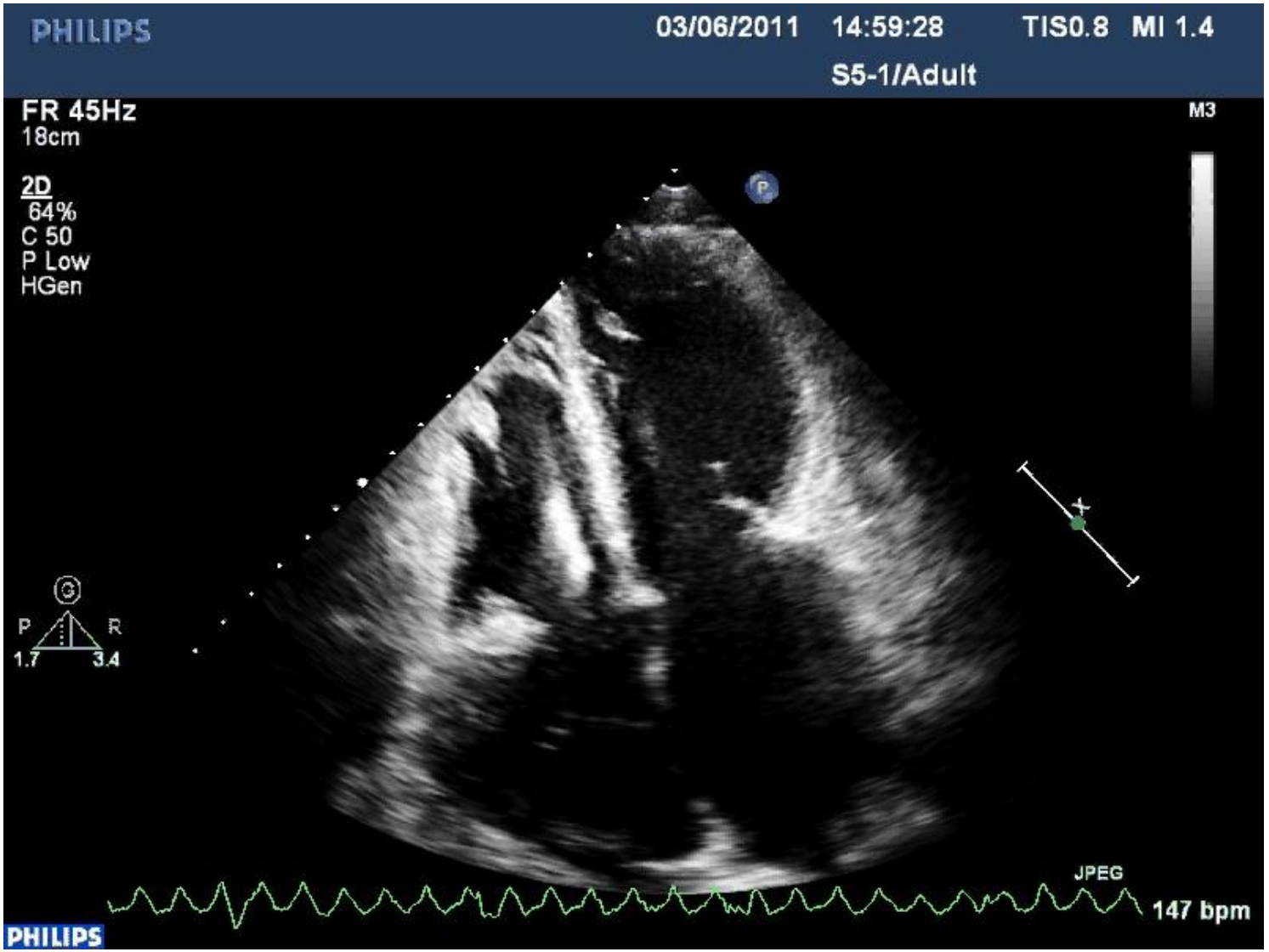
- Patient was followed by his cardiologist for the last four years. He now presents with aggravated fatigue and breathlessness already occurring during daily activities

- Physical exam:
  - 171cm, 73 kg (BMI 25)
  - blood pressure 90/60mmHg, Heart rate 55 irregular
  - Positive hepatojugular reflux
  - 2/6 cardiac murmur
  - lungs free,
  - extremities: cold
  - no edema

ECG



Echocardiography



Labs

Creatinin	141 mmol/L
BUN	14 mmol/L
Sodium	141 mmol/L
Potassium	4.7 mmol/L
C-reactive protein	2 mg/L
Albumin	37 g/L
B-type natriuretic peptide (BNP)	2071 ng/L
ASAT	35 U/L
ALAT	24 U/L
GGT	192 UL

Labs

Hemoglobin	162 g/L
MCV	91 fl
MCH	29 pg
MCHC	321 g/L
Hematocrite	50
Reticulocytes	17 ‰
Hypochrome EC	15 % (< 5%)

Iron status

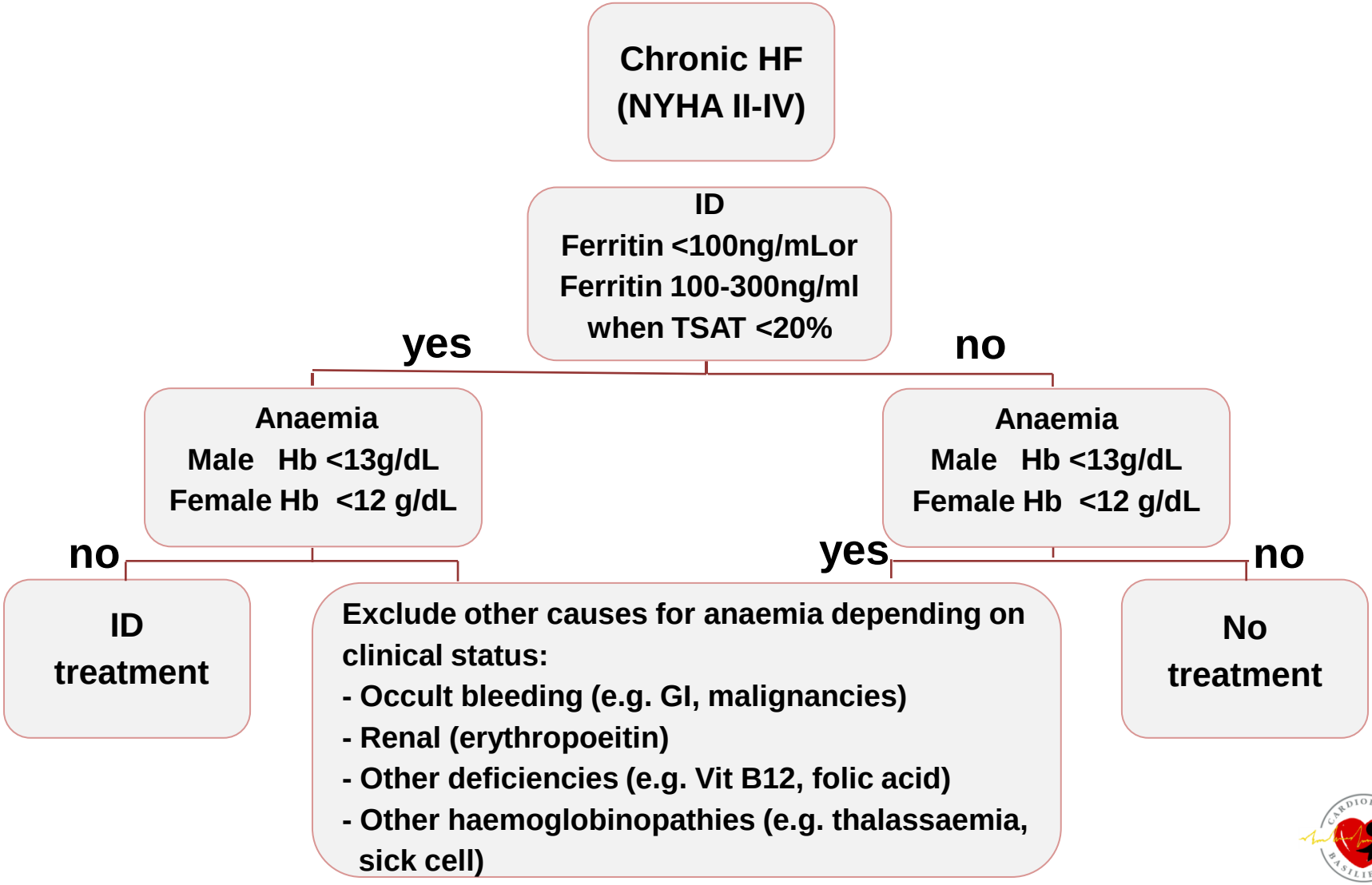
Iron	11 umol/L	(11-38)
Ferritin	27 ug/L	(30-300)
Transferrin	3.4 g/L	(2-3.6)
Transferrin saturation (Tsat)	13%	(16-45)
Soluble transferrin receptor	7.7 mg/L	(2.2-5.0)

Diagnosis of iron deficiency

Variable	ACD	ID	ACD & ID
Tsat	< 20%	< 20%	< 20%
Ferritin	> 100	< 30	30 - 100
sTfR	normal	increased	normal to increased
Ratio sTfR / log ferritin	low (<1)	high (>2)	high (>2)

ACD = anemia of chronic disease; ID = iron deficiency;
Tsat = transferrin saturation; sTfR = soluble transferrin receptor

Diagnostic algorithm



Iron substitution: How ???

1. Food

2. Oral iron substitution

3. i.v. iron substitution

Problems with oral iron substitution

1. Malabsorbtion due to oedema of the gastrointestinal mucosa
2. Gastrointestinal side effects
3. Poor long-term compliance
4. Fails to efficiently replenish iron stores as measured by serum ferritin and transferrin saturation

Clinical trials with i.v. iron substitution in CHF

- Bolger AP et al, J Am Col Cardiol, 2006 — 200mg/3x/week
- Toblli JE et al, J Am Col Cardiol, 2007 — 200mg/week
- Okonko DO et al, J Am Col Cardiol, 2008 — 200mg/week
- Usmanov RI et al, J Nephrol, 2008 — 100mg/week
- Anker SD et al, N Engl J Med, 2009 — 200mg/week

→ Decision to infuse 200mg i.v. iron (ferric carboxymaltose) / week for three weeks

Clinical trials with i.v. iron substitution in CHF

- The safety and efficacy of high dose bolus injection (500-1000mg iron/10ml) is currently addressed in ongoing clinical trials
    - **CONFIRM** FAIR-**HF**
    - **EFFECT HF**

3 months after iron substitution

i.v. iron substitution	*before*	*after*
Iron	11 umol/L	24 umol/L
Ferritin	27 ug/L	38 umo/L
Transferrin	3.4 g/L	3.2 g/L
Transferrin saturation (Tsat)	13%	30%
Soluble transferrin receptor	7.7 mg/L	5.2 mg/L
Hemoglobin	162 g/L	174 g/L
Hemotocrite	50%	52%
MCV	91 fl	95 fl
MCH	29 pg	32 pg
MCHC	321 g/L	334 g/L
Hypochrome EC	15 %	7%

Clinical status after i.v. iron substitution

- Subjective improvement of physical activity and fatigue
- Improvement of NYHA class: from III to II-III
- Objective improvement of exercise capacitiy
  - Increase in peak VO2 from 9 ml/min/kg to 12 ml/min/kg
- No rehospitalization
- Patient will be evaluated for HTx

Thank you

Alberto Giacometti: Walking man